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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/122,144	07/24/98	BLUMBERG R	B0801/7117

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EXAMINER	
EWOLDT, G	
ART UNIT	**PAPER NUMBER**
1644	23

DATE MAILED: 06/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary

Application No.	Applicant(s)
09/122,144	Blumberg et al.
Examiner	**Art Unit**
G. R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *2/05/01, 4/10/01, and 6/07/01*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *25-60* is/are pending in the application.

4a) Of the above, claim(s) *35-60* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *25-34* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *18, 21*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. In view of Applicant's amendments, response, and declaration, filed 2/05/01, 4/10/01, and 6/07/01, only the following rejections remain.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 25-31 and 33-34 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 92/05793, for the reasons of record, as set forth in Paper No. 13, mailed 5/10/00.

Applicant's arguments, filed 2/05/01, have been fully considered but have not been found persuasive. Applicant argues that the bispecific binding agent of the reference is aimed at the Fc-γ, and not the FcRn receptor. Applicant further argues that the binding agents of the reference comprise different antibody fragments than does the preparation of the instant claims. Applicant argues that "most of the embodiments of proposed by Medarex (and perhaps all) have no FcRn binding moiety." Applicant also argues that "Medarex teaches a conjugate of an antigen and an Fc-γ binding partner." Applicant also includes several arguments regarding the recitation of oral, nasal, and aerosol formulations and argues that these limitations are not taught by the prior art. However, Applicant's arguments can not overcome the specific teaching of the reference which teaches "an antigen can be coupled to an antibody, or fragment thereof, specific for an Fc receptor of an antigen presenting cell." As the reference further teaches a hepatitis antigen and IgG antibodies, the reference teaches the limitations of the claims because all IgG antibodies inherently comprise the FcRn binding partner of the instant claims because said IgG's comprise an Fc region which inherently binds the FcRn. Further teachings of the reference, or "most of the embodiments" of the reference are irrelevant. Applicant admits that "Medarex teaches a conjugate of an antigen and an Fc-γ binding partner," thus, Applicant essentially admits that the reference teaches the claimed invention because an Fc-γ binding partner would also be an FcRn binding partner if said binding partner comprises an IgG.

Regarding the arguments to an in oral, aerosol, or nasal formulation, said "formulation" adds no patentable weight to the claims absent the recitation of a component of said formulation that would delineate said formulation from a formulation that might be administered by other routes including intramuscular or intravenous, as evidenced by U.S. Patent No. 6,187,757 which teaches that large fusion proteins can be administered by various routes including oral, aerosol, nasal, dermal, intradermal, intravenous, subcutaneous, etc (see particularly column 81, line 65 - column 82, line 15). Also see U.S. Patent No. 5,948,892 which teaches that a chemokine-IgFc fusion protein can be administered by various routes including oral, nasal, intradermal, intravenous, intramuscular, etc (see particularly column 5, lines 29-37 and column 6, lines 52-65).

4. The following are New Grounds for Rejection.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 25-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that, other than an Fc fragment (or region) of IgG, Applicant was in possession of an FcRn binding partner. The specification defines FcRn binding partner as "any entity that can be specifically bound by the FcRn with consequent active transport by the FcRn of the FcRn binding partner." However, the only examples of said FcRn binding partner are IgG's or fragments of IgG's, all comprising the IgG Fc region. The specification further defines regions of the IgG Fc fragment required for binding. The specification fails to disclose, however, whether or not other FcRn binding partner actually exist, as the specification discloses no antibodies specific for FcRn, no specific "mimics of the foregoing", nor any specific "FcRn binding partners selected from molecularly diverse libraries." Absent any description of any specific FcRn binding partner other than an Fc fragment of Ig, one of skill in the art would conclude that the specification

fails to disclose a representative number of species to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 25-34 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,428,130 (1995, of record) in view of WO 92/05793 (of record).

The '130 patent teaches a pharmaceutical preparation comprising a fusion protein comprising a ligand of interest and an Fc fragment of IgG (see particularly column 10, lines 19-49, and column 11, line 1), said pharmaceutical preparation further comprising an oral formulation including a solid and liquid (elixir), or an aerosol formulation for inhalation. The reference further teaches that the choice of properties such as dosages and routes of administration are dependent on the properties of the hybrid protein being used and that the choice of the most advantageous set of properties is "well within the skill of the physician" (see particularly column 31, lines 3-48). The reference further teaches that the IgG portion of the fusion protein provides increased plasma stability and half-life for the ligand of interest (see particularly column 5, lines 15-23). Additionally, the reference teaches that said pharmaceutical preparation is particularly useful for the treatment of individuals in need of antiviral therapy (see particularly column 6, paragraph 2).

The '130 application differs from the claimed invention in that it does not teach a pharmaceutical preparation comprising a hepadnaviridae antigen as the specific ligand of interest.

WO 92/05793 teaches a pharmaceutical preparation for activating an immune response comprising a conjugate of a hepadnaviridae (hepatitis) (see claims 8-9) antigen, an Fc binding fragment of IgG, and a pharmaceutically acceptable carrier including saline (see particularly page 3, paragraphs 1-2, page 7, paragraph 4, and page 9, line 5).

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to prepare a pharmaceutical preparation with increased plasma stability and plasma half-life comprising a fusion protein comprising a ligand of interest and an Fc fragment of IgG, said pharmaceutical preparation further comprising an oral formulation including a solid and liquid (elixir), or an aerosol formulation for inhalation, as taught by the '130 patent, substituting a hepatitis antigen as the ligand of interest, as taught by the '869 application. One of ordinary skill in the art would have been motivated to substitute hepatitis as the ligand of interest, as taught by the '869 application, in the fusion protein of the '130 patent, to create a pharmaceutical preparation for the treatment of the well-known hepatitis pathogen, particularly in view of the teaching of the '130 patent that said pharmaceutical preparation is particularly useful for the treatment of individuals in need of antiviral therapy. Claim 32 is included in the rejection because the use of a propellant for the delivery of an aerosol formulation is well within the purview of one of ordinary skill in the art at the time the invention was made and adds no patentable weight to the invention. Claim 34 is included because absent a claim of sterility, the pharmaceutical preparation would necessarily be nonaseptic.

Note that Applicant has submitted arguments and a declaration against a previous 35 U.S.C. 103(a) rejection, however, that rejection has been withdrawn and the arguments are not relevant to the instant rejection.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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June 14, 2001

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